Effect of Vitamin E and Selenium on Incidence of Physician-Diagnosed COPD: The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

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Rationale: Vitamin E and selenium play a role in antioxidant defenses and may decrease oxidant damage to tissues and thereby reduce the risk of COPD. Prior observational epidemiologic studies support this hypothesis, but no large randomized trials have assessed supplementation with selenium, and one trial (Heart Protection Study) found no effect of combined vitamins E, C and beta-carotene on COPD hospitalizations. The effect of selenium, vitamin E or both on COPD risk was assessed in the Selenium and Vitamin E Cancer Prevention Trial (SELECT).

Methods: SELECT was a double-blind, randomized, placebo-controlled trial of 35,533 men (median age 62.4 yrs) at 427 sites in the US, Canada, and Puerto Rico testing the single or joint effects of vitamin E (400 IU/day *all rac*-α-tocopherol acetate) and selenium (200 μg/d selenomethionine) in a 2x2 factorial design. As of 10/23/08, the end of supplementation in SELECT, the median length of follow-up was 5.46 years (range 4.17-7.33 years). The endpoint for the current study was assessed by participant report on bi-annual medical history questionnaires of incident physician-diagnosed emphysema, COPD and/or chronic bronchitis in 32,371 eligible men [excluding men with inadequate data (2,094) or with prevalent lung disease at baseline (1,068)].

Results: Hazard ratios [95% confidence intervals (CIs)] for COPD were 1.08 (95% CI 0.91, 1.28) for vitamin E, 1.01 (95% CI 0.85, 1.20) for selenium, and 0.94 (95% CI 0.79, 1.12) for combined vitamin E and selenium, all versus placebo/placebo. Findings were unchanged in models that included participants with a baseline report of prevalent lung disease, and Kaplan-Meier curves show no separation over time in probability of event by treatment group. The cumulative incidence of COPD was 3.27% over the follow-up period, and current smokers were at increased risk compared to never smokers (HR 7.22; 95% CI 5.99, 8.72).

Conclusion: Selenium or vitamin E, alone or in combination, did not prevent COPD in a population of relatively healthy men. Although it is possible that effects may have been missed due to the short duration of treatment and suboptimal endpoint ascertainment, this

study is a strong test of the hypothesis that antioxidants decrease the risk of physician-diagnosed COPD. Statistical power to test for subgroup effects in smokers is limited, although such a test follows directly from the study hypothesis. A spirometry endpoint, currently being evaluated, may give further insight into these questions in a subgroup enriched with smokers.